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An increase in contamination of agricultural commodities with mycotoxins forceful by climate change becomes an intractable problem worldwide, alarming intercontinental food security. On the other hand, to lessen the use of agrochemicals, seeking environmentally-safe antimycotoxin agents is urgent action. This current study aims at elucidating the antifungal and antimycotoxin modes of action of main active stilbenoid molecules derived from vine by-product extracts via treatments with *Fusarium graminearum* fungus – the primary causal agent of *Fusarium* Head Blight of wheat and the main producer of type B trichothecene (TCTB) mycotoxin. A monomer resveratrol (RES, 35 μM) and a tetramer vitisin B (VIT B, 8 μM) were the two designated candidates due to their predominance in the extracts. An array of the *in vitro* fungicidal bioactivities of the molecules, consisting of anti-spore germination, and inhibition of biomass production and TCTB yield, were proved in which the fungus was significantly susceptible to VIT B rather than RES. To deeper understand their modes of action underlying the antifungal and antimycotoxin activities, multi-omics approaches including mRNA-seq-based transcriptomics and LC-MS/MS-based nontargeted metabolomics were performed. The mRNA-seq data illustrated a significantly fungal global transcriptomic regulation induced by VIT B. Approximately 7,000 genes were differentially expressed upon exposure to VIT B compared to the untreated control at both 3 and 5 days post inoculation (dpi), while a very slight fungal transcriptomic regulation was observed for RES. In conjunction with metabolomics data, our study provided comprehensive insights into the modes of action of the active molecule VIT B. These findings hold promise for developing novel biofungicides exploiting viticulture wastes in order to contribute to lowering the contamination of cereals with mycotoxins and add value to the undervalued vine by-products.